

WE CLAIM:

1. A modified oligonucleotide having formula (III):

Peptide - L - Oligon (III)

wherein L is a linker or a bond, Peptide is any amino acid sequence, and Oligon is an

5 oligonucleotide or analog thereof.

2. A composition comprising the modified oligonucleotide of claim 1 or a pharmaceutically acceptable salt thereof.

- 10 3. The composition of claim 2 further comprising an antibiotic.

4. The modified oligonucleotide of claim 1 wherein L comprises at least one of the following: 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (SMCC), 6-aminohexanoic acid (AHEx), 4-aminobutyric acid, 4-aminocyclohexylcarboxylic acid, polyethylene glycol, any amino acid, or any combination thereof.

5. A modified peptide nucleic acid (PNA) molecule having formula (I):

Peptide - L - PNA (I)

- 20 wherein L is a linker or a bond, Peptide is any amino acid sequence, and PNA is a peptide nucleic acid.

6. The modified PNA molecule of claim 5 wherein Peptide is a cationic peptide or peptide analog or a functionally similar moiety having formula (II):

25 C-(B-A)_n-D, (II)

wherein:

A is from 1 to 8 non-charged amino acids and/or amino acid analogs;

B is from 1 to 3 positively charged amino acids and/or amino acid analogs;

C is from 0 to 4 non-charged amino acids and/or amino acid analogs;

30 D is from 0 to 3 positively charged amino acids and/or amino acid analogs; and

n is 1-10;

wherein the total number of amino acids and/or amino acid analogs is from 3 to 20.

7. The modified PNA molecule of claim 5 wherein L comprises at least one of the following: 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (SMCC), 6-aminohexanoic acid (AHEx), 4-aminobutyric acid, 4-aminocyclohexylcarboxylic acid, polyethylene glycol, any amino acid, or any combination thereof.
8. The modified PNA molecule of claim 7 wherein L comprises a combination of β .ALA or ADO and any one of SMCC, AHEx, 4-aminobutyric acid, 4-aminocyclohexylcarboxylic acid, polyethylene glycol, and any amino acid.
9. The modified PNA molecule of claim 8 wherein L is selected from the group consisting of: -achc- β .ala-, -achc-ado-, -lcsbcc- β .ala-, -mbs- β .ala-, -emcs- β .ala-, -lcsbcc-ado-, -mbs-ado-, -emcs-ado- or -smph-ado-.
10. The modified PNA molecule of claim 5 wherein A comprises from 1 to 6 non-charged amino acids and/or amino acid analogs and B comprises 1 or 2 positively charged amino acids and/or amino acid analogs.
11. The modified PNA molecule of claim 10 wherein A comprises from 1 to 4 non-charged amino acids and/or amino acid analogs.
12. The modified PNA molecule of claim 5 wherein the positively charged amino acids and amino acid analogs are selected from the group consisting of lysine, arginine, diamino butyric acid (DAB) and ornithine.
13. The modified PNA molecule of claim 5 wherein the non-charged amino acids and amino acid analogs are selected from the group consisting of Ala, Val, Leu, Ile, Pro, Phe, Trp, Met, Gly, Ser, Thr, Cys, Tyr, Asn, Gln and the non-naturally occurring amino acids 2-aminobutyric acid, β -cyclohexylalanine, 4-chlorophenylalanine, norleucine, and phenylglycine.
14. The modified PNA molecule of claim 5 wherein the non-charged amino acids and amino acid analogs are selected from the group consisting of Ala, Val, Leu, Ile, Pro, Phe, Trp, Met and the non-naturally occurring non-polar amino acids β -cyclohexylalanine, 4-chlorophenylalanine, and norleucine.

15. The modified PNA molecule of claim 5 wherein the total number of amino acids and/or amino acid analogs is 15 or less.
16. The modified PNA molecule of claim 5 wherein the total number of amino acids and/or amino acid analogs is 12 or less.
17. The modified PNA molecule of claim 5 wherein the total number of amino acids and/or amino acid analogs is 10 or less.
18. The modified PNA molecule of claim 5 wherein the Peptide is (KFF)₃K (SEQ ID NO: 161) or subunits thereof comprising at least 3 amino acids.
19. The modified PNA molecule of claim 18 wherein the Peptide is (KFF)₃ (SEQ ID NO: 1).
20. The modified PNA molecule of claim 5 wherein the Peptide is selected from the group consisting of FFRFFRFFR (SEQ ID NO: 6), LLKLLKLLK (SEQ ID NO: 7), LLRLLRLLR (SEQ ID NO: 8), LLKKLAKAL (SEQ ID NO: 9), KFKVKFVVKK (SEQ ID NO: 11), LLKLLKLLK (SEQ ID NO: 12), LLKKLAKALK (SEQ ID NO: 13), RRLFPWWPFRRVC (SEQ ID NO: 14), GRRWPWWPWKWPLIC (SEQ ID NO: 15), LVKKVATTLKKIFSKWKC (SEQ ID NO: 16), KKFKVKFVVKKC (SEQ ID NO: 17), and any subunit thereof comprising at least 3 amino acids, wherein at least one amino acid is a positively charged amino acid.
21. A modified PNA molecule comprising:
H-KFFKFFKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 24),
H-FFKFFKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 25),
H-FKFFKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 26),
H-KFFKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 27),
H-FFKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 28),
H-FKFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 29),
H-KFFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 30),
H-FFK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 31),
H-FK-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 32),

- 5 H-K-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 33),
H-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 34),
H-KFFKFFKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 35),
H-FFKFFKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 36),
H-FKFFKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 37),
H-KFFKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 38),
H-FFKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 39),
H-FKFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 40),
H-KFF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 41),
10 H-FF-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 42),
H-F-ado-CATAGCTGTTTC-NH₂ (SEQ ID NO: 43),
H-KFFKFFKFFK-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 18),
H-KFFKFFKFFK-ado-TGA CTA GAT GAG-NH₂ (SEQ ID NO: 44),
H-KFFKFFKFFK-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 45),
15 H-FFKFFKFFK-GGC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 53),
H-FFRFFRFFR-GGC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 54),
H-LLKLLKLLK-GGC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 55),
H-LLRLLRLLR-GGC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 56),
H-LLKKLAKALK-GC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 57),
20 H-KRRWPWWPWKK-C-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 58),
H-KFKVKFVVKK-GC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 59),
H-LLKLLKLLK-C-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 60),
H-FFKFFKFFK-GGC-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 61),
H-KFFKFFKFFK-C-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 62),
25 H-F-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 63),
H-FF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 64),
H-KFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 65),
H-FKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 66),
H-FFKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 67),
30 H-KFFKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 68),
H-FKFFKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 69),
H-FFKFFKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 70),
H-KFFKFFKFF-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 71),
H-LLKKLAKALKG-ahex-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 21),

- 5 H-LLKKLAKALKG-ado-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 72),
H-KFFKFFKFFK-ado-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 73),
H-KFFKFFKFFK-ahex-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 74),
H₂N-KFFKFFKFFK-C-smcc-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 75),
H₂N-LLKKLAKALK-GC-smcc-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 76),
H₂N-KFFKFFK-C-smcc-ado-CCA TCT AAT CCT-NH₂ (SEQ ID NO: 77),
H-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 78),
H₂N-KFFKVKFVVKK-C-smcc-ado-TTC AAA CAT AGT-NH₂ (SEQ ID NO: 79),
H₂N-KFFKVKFVVKK-C-smcc-ado-TTG TGC CCC GTC-NH₂ (SEQ ID NO: 80),
10 H₂N-KKFKVKFVVKKC-achc-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 81),
H-KFFKFFKFFK-achc-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 82),
H₂N-KKFKVKFVVKKC-lcsmcc-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 83),
H₂N-KKFKVKFVVKKC-mbs-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 84),
H₂N-KKFKVKFVVKKC-emcs-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 85),
15 H₂N-KKFKVKFVVKKC-smph-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 86),
H₂N-KKFKVKFVVKKC-amas-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 87),
H₂N-KKFKVKFVVKKC-smpb-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 88),
H₂N-KKFKVKFVVKKC-lcsmcc-gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 89),
H₂N-KKFKVKFVVKKC-lcsmcc-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 90),
20 H₂N-KKFKVKFVVKKC-lcsmcc-β.cypr-TTCAAACATAGT-NH₂ (SEQ ID NO: 91),
H₂N-KKFKVKFVVKKC-lcsmcc-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 92),
H₂N-KKFKVKFVVKKC-lcsmcc-adc-TTCAAACATAGT-NH₂ (SEQ ID NO: 93),
H-KFFKFFKFFK-ado-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 94),
H-KFFKFFKFFK-ado-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 95),
25 H-KFFKFFKFFK-ado-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 96),
H-KFFKFFKFFK-ado-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 97),
H-KFFKFFKFFK-ado-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 98),
H-KFFKFFKFFK-ado-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 99),
H-KFFKFFKFFK-Gly-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 100),
30 H-KFFKFFKFFK-Gly-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 101),
H-KFFKFFKFFK-Gly-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 102),
H-KFFKFFKFFK-Gly-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 103),
H-KFFKFFKFFK-Gly-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 104),

- 5 H-KFFKFFKFFK-Gly-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 105),
H-KFFKFFKFFK-P-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 106),
H-KFFKFFKFFK-P-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 107),
H-KFFKFFKFFK-P-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 108),
H-KFFKFFKFFK-P-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 109),
H-KFFKFFKFFK-P-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 110),
H-KFFKFFKFFK-P-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 111),
H-KFFKFFKFFK-aha-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 112),
H-KFFKFFKFFK-aha-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 113),
10 H-KFFKFFKFFK-aha-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 114),
H-KFFKFFKFFK-aha-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 115),
H-KFFKFFKFFK-aha-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 116),
H-KFFKFFKFFK-aha-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 117),
H-KFFKFFKFFK-β.ala-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 118),
H-KFFKFFKFFK-β.ala-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 119),
H-KFFKFFKFFK-β.ala-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 120),
H-KFFKFFKFFK-β.ala-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 121),
H-KFFKFFKFFK-β.ala-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 122),
H-KFFKFFKFFK-β.ala-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 123),
20 H-KFFKFFKFFK-P-p-TTCAAACATAGT-NH₂ (SEQ ID NO: 124),
H-KFFKFFKFFK-P-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 125),
H-KFFKFFKFFK-K-K-TTCAAACATAGT-NH₂ (SEQ ID NO: 126),
H-KFFKFFKFFK-F-F-TTCAAACATAGT-NH₂ (SEQ ID NO: 127),
H-KFFKFFKFFK-F-K-TTCAAACATAGT-NH₂ (SEQ ID NO: 128),
H-KFFKFFKFFK-K-F-TTCAAACATAGT-NH₂ (SEQ ID NO: 129),
25 H-KFFKFFKFFK-phg-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 130),
H-KFFKFFKFFK-phg-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 131),
H-KFFKFFKFFK-phg-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 132),
H-KFFKFFKFFK-phg-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 133),
H-KFFKFFKFFK-phg-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 134),
30 H-KFFKFFKFFK-phg-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 135),
H-KFFKFFKFFK-achc-ado-TTCAAACATAGT-NH₂ (SEQ ID NO: 136),
H-KFFKFFKFFK-achc-Gly-TTCAAACATAGT-NH₂ (SEQ ID NO: 137),

H-KFFKFFKFFK-achc-P-TTCAAACATAGT-NH₂ (SEQ ID NO: 138),

H-KFFKFFKFFK-achc-aha-TTCAAACATAGT-NH₂ (SEQ ID NO: 139),

H-KFFKFFKFFK-achc-β.ala-TTCAAACATAGT-NH₂ (SEQ ID NO: 140) or

H-KFFKFFKFFK-achc-achc-TTCAAACATAGT-NH₂ (SEQ ID NO: 141).

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22. The modified PNA molecule of claim 5 wherein the PNA sequence is complementary to at least one nucleotide sequence in a bacterium.

23. The modified PNA molecule of claim 22 wherein the PNA sequence is complementary to at least one ribosomal RNA sequence, messenger RNA sequence, or DNA sequence in said bacterium.

24. The modified PNA molecule of claim 5 wherein the PNA sequence is in a parallel or anti-parallel orientation.

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25. The modified PNA of claim 22 wherein said at least one nucleotide sequence is essential for the survival of said bacterium and said PNA sequence inhibits the function of said at least one nucleotide sequence.

26. The modified PNA molecule of claim 5 wherein said PNA sequence comprises from 5 to 20 nucleobases.

27. The modified PNA molecule of claim 5 wherein said PNA sequence comprises from 7 to 15 nucleobases.

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28. The modified PNA molecule of claim 5 wherein said PNA sequence comprises from 8 to 12 nucleobases.

29. A modified PNA molecule comprising:
H-KFFKFFKFF-ado-JTJTJJT-ado-ado-ado-TCCCTCTC-Lys-NH₂ (SEQ ID NO: 22),
H-KFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 46),
H-FKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 47),
H-FFKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 48),
H-KFFKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 49),

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H-FKFFKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 50),
H-FFKFFKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 51), or
H-KFFKFFKFF-ado-JTJTJJT-ado-ado-ado-TCCTCTC-Lys-NH₂ (SEQ ID NO: 52).

- 5 30. A composition comprising the modified PNA molecule of claim 5 or a pharmaceutically acceptable salt thereof.
31. The composition of claim 30 further comprising an antibiotic.
- 10 32. A composition comprising two or more modified PNA molecules of claim 5 or pharmaceutically acceptable salts thereof.
33. The composition of claim 32 further comprising an antibiotic.
- 15 34. A method of treating an infectious disease in a mammal comprising administering an effective amount of a modified PNA molecule of claim 5 to said mammal.
35. The method of claim 34 wherein said infectious disease is a bacterial infection.
- 20 36. A method of treating an infectious disease in a mammal comprising administering an effective amount of modified oligonucleotide of claim 1 to said mammal.
37. The method of claim 36 wherein said infectious disease is a bacterial infection.
- 25 38. A method of treating an infectious disease in a mammal comprising administering an effective amount of a composition of claim 30 to said mammal.
39. A method of treating an infectious disease in a mammal comprising administering an effective amount of a composition of claim 32 to said mammal.
- 30 40. A method of identifying a PNA sequence in a PNA molecule useful for inhibiting or reducing growth of at least one bacterium comprising:

contacting a first bacterium with a first modified PNA molecule of claim 5 having a first PNA sequence, wherein said PNA sequence is complementary to at least one nucleotide sequence in said first bacterium;

contacting a second bacterium with a second modified PNA molecule of claim 5 having a second PNA sequence, wherein said PNA sequence is complementary to at least one nucleotide sequence in said second bacterium; and

identifying which PNA sequence is more effective in inhibiting or reducing growth of said bacterium.

41. The method of claim 40 wherein said first and second PNA molecules are identical except for said PNA sequence, and said first and second bacterium are the same species.

42. A method for disinfecting a non-living object comprising contacting said object with a modified oligonucleotide of claim 1.

43. A method for disinfecting a non-living object comprising contacting said object with a modified PNA molecule of claim 5.

44. A method for disinfecting a non-living object comprising contacting said object with a composition comprising a modified oligonucleotide of claim 1.

45. A method for disinfecting a non-living object comprising contacting said object with a composition comprising a modified PNA molecule of claim 5.

46. The method of claim 42 wherein said object is a surgery tool, hospital inventory, dental tool, slaughterhouse inventory, slaughterhouse tool, dairy inventory, or dairy tool.

47. The method of claim 43 wherein said object is a surgery tool, hospital inventory, dental tool, slaughterhouse inventory, slaughterhouse tool, dairy inventory, or dairy tool.